Health Advisory:

Non-Safety-Related Voluntary Recall of Unused Doses from Certain Lots of Sanofi Pasteur H1N1 Vaccine in Pre-Filled Syringes

01-30-2010

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Health Advisory
01-30-2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: Non-Safety-Related Voluntary Recall of Unused Doses from Certain Lots of Sanofi Pasteur H1N1 Vaccine in Pre-Filled Syringes

This is an official
CDC HEALTH UPDATE

Distributed via Health Alert Network
Friday, January 29, 2010 19:15 ET (7:15 PM ET)

Summary: As part of its quality assurance program, Sanofi Pasteur, Inc., performs routine, ongoing testing of influenza vaccines after the vaccine has been distributed to health care providers to ensure that the vaccine continues to meet required specifications. In recent testing of its influenza A (H1N1) monovalent vaccine, Sanofi Pasteur found five distributed lots of single-dose, pre-filled syringe pediatric (0.25 mL) vaccine and one distributed lot of single-dose pre-filled syringe for older children and adults (0.5 mL) vaccine had potency below pre-specified limits. The manufacturer is conducting a non-safety related voluntary recall of any unused doses of these affected lots of vaccine. Information will be sent by Sanofi Pasteur to providers who received vaccine from the affected lots.

Background

After performing routine tests, Sanofi Pasteur notified the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) that the potency in five lots of pediatric pre-filled syringes and one lot of adult pre-filled syringes that had been distributed to providers was later found to have dropped below a pre-specified limit.

Recommendations

While the potency of these lots is now below the manufacturer's specification for the product, CDC and FDA are in agreement that the small decrease in antigen content is unlikely to result in a clinically significant reduction in immune response among persons who have received the vaccine. For this reason, there is no need to revaccinate persons who have received vaccine from these lots.

Providers will be asked to return any unused vaccine from the affected lots to the manufacturer. The only vaccine affected by this recall is supplied in pre-filled syringes and is identified by the following lot numbers:

UT023AA, UT023BA, UT023CA, UT023EA, UT023FA

(NDC # 49281-650-25, which also may be recorded as # 49281-0650-25), 0.25 mL syringes in 10-packs

UT037AA

(NDC # 49281-650-90, which also may be recorded as # 49281-0650-90), 0.5 mL syringes in 25-packs

These lots were shipped to providers between November 2009 and January 2010. Sanofi Pasteur will send directions for returning unused vaccine from these lots to providers.

All vaccines are thoroughly tested prior to release and shipping for safety, purity, and potency. The affected lots met all required specifications at the time of release. CDC and FDA have determined that there are no safety concerns for people who have received these vaccines.

The potency of the affected lots of vaccine is only slightly below the specification limit. Vaccine doses from these lots are still expected to be effective in stimulating a protective response. There is no need to re-administer a dose to those who received vaccine from these lots.

As is recommended for all 2009 H1N1 vaccines, all children less than 10 years old should get the recommended two doses of H1N1 vaccine approximately a month apart for the optimal immune response. So, children less than 10 years old who have only received one dose of vaccine thus far should still receive a second dose of 2009 H1N1 vaccine.

For children 6 months of age and older, vaccine is available in multidose vials. The vaccine in multidose vials is safe and effective vaccine for children. The standard dose for this preparation for administration to infants 6-35 months old is the same as for the pre-filled syringes, 0.25 mL. For healthy children at least 2 years of age, the nasal spray (live, attenuated influenza vaccine) is also an option. The nasal spray vaccine is produced in single units that do not contain thimerosal.

Sanofi Pasteur has informed the CDC that it will be submitting a field correction to the FDA to request a change for the expiration date of the company's remaining pediatric and adult pre-filled syringes. CDC will share additional information as soon as it is available.

For More Information:

Call CDC's toll-free information line, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, which is available 24 hours a day, every day.

Categories of Health Alert Messages:	
Health Alert	Conveys the highest level of importance; warrants immediate action or attention.
Health Advisory	Provides important information for a specific incident or situation; may not require immediate action.
Health Update	Provides updated information regarding an incident or situation; unlikely to require immediate action.

##This Message was distributed to State and Local Health Officers, Public Information Officers, Epidemiologists and HAN Coordinators as well as Clinician organizations##

CDCHAN-000306-2010-01-29-UPD-N

Non-Safety-Related Voluntary Recall of Unused Doses from Certain Lots of Sanofi Pasteur H1N1 Vaccine in Pre-Filled Syringes

Health Advisory:

Interim Recommendations from CDC for Initial Domestic Medical Screening of Haitian Orphan

Date: February 9, 2010

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Advisory
February 9, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Interim Recommendations from CDC for Initial Domestic Medical Screening of Haitian Orphans**

Purpose: To provide medical screening recommendations for diseases of public health importance in orphaned children entering the United States from Haiti under humanitarian parole status.

Target Audience: Domestic medical providers evaluating orphaned children being evacuated from Haiti

Background

The January 12, 2010, earthquake and multiple aftershocks created enormous devastation and loss of life in the heavily populated city of Port-au-Prince, Haiti, and outlying areas. *Although the exact numbers of deaths is still unknown it is estimated that more than 200,000 people lost their lives since the event.* There was an estimated 380,000 orphans in Haiti as of 2007, but since the earthquake this number is unknown. The health status of orphans in Haitian orphanages is considered very poor. Even before the earthquake, Haiti had a high prevalence of *bacterial and protozoal diarrhea, hepatitis A and E, typhoid fever, dengue fever, malaria, leptospirosis, tuberculosis, and HIV.* On January 18, 2010, the Department of Homeland Security (DHS) announced a humanitarian parole policy allowing orphaned children from Haiti to enter the United States to ensure that they receive the care they need.

Normally, before admission to the United States, all internationally adopted children are required to have a medical examination in their country of origin, specified by CDC, performed by a physician designated by the Department of State. However, given the urgency of the current situation, Haitian orphans entering the United States under parole status have been allowed to bypass this overseas medical screening examination prior to departure. *Therefore, this document presents recommendations for screening for communicable diseases of public health importance. It is meant to take the place of the overseas medical screening exam, referred to hereafter as the initial domestic medical screening for orphan parolees.* This medical screening should be performed as soon as possible after arrival and consist of a general medical screening, as well as screening for tuberculosis (TB), vaccination status, HIV, intestinal parasites, malaria, syphilis and mental health. A subsequent more comprehensive medical evaluation is recommended in accordance with the American Academy of Pediatrics guidelines on the Medical Evaluation of Internationally Adopted Children for Infectious Diseases (Red Book®: 2009 Report of the Committee on Infectious Diseases - 28th Ed. 2009).

Although these examinations may be performed together, the immediate screening described in this document should not be delayed to accommodate the comprehensive examination.

Initial Medical Screening

All orphans should have a medical history (if known) and physical examination.

Components of the medical history should include:

- History of trauma
- Symptoms of communicable disease (i.e. fever, coryza, cough, rash, diarrhea, vomiting)
- Past medical and surgical history, including any known chronic diseases
    - Specific history of TB and HIV should be solicited
    - Medication history

Components of the physical examination should include:

- Vital signs and assessment of hydration status
- Height, weight, head circumference (if age appropriate)
- Obvious injuries that may have resulted from trauma
- A full physical examination with particular attention paid to signs that may indicate underlying medical problems such as heart disease, asthma, chronic malaria (e.g. tachycardia, heart murmurs, labored respirations, abdominal tenderness) or undetected but subtle injury from trauma (e.g. splenic rupture).
- Assessment of nutritional status (looking for signs of malnutrition)

If fever is present, there should be a high clinical suspicion of malaria, dengue fever, and typhoid. Consideration should also be given to detecting clinical conditions requiring isolation (i.e. typhoid, TB, measles or chickenpox). Optimally, evaluation should be performed in consultation with an expert in infectious diseases or tropical medicine.

Orphans with known chronic medical conditions (e.g. asthma, congenital cardiac conditions, seizure disorders) should be carefully evaluated and treated, particularly since previous therapy may have been disrupted. Orphans with known chronic cardiac and respiratory disease should have vital signs assessed, including oxygen saturation (portable oximeter) as soon as possible. Orphans with diabetes should have a glucose measurement as soon as possible.

Further, in 2009, the Haitian National Nutrition Survey found acute and chronic malnutrition to be 4.5% and 24-35%, respectively.

Laboratory screening tests should include:

- Complete blood cell count with red blood cell indices
- HIV testing
- Malaria smear (if symptomatic)
- Stool examination for ova and parasites (3 specimens)
- Stool examination for *Giardia spp., Cryptosporidium*, rotavirusantigen (if symptomatic); strongyloides serology if eosinophilia

- Syphilis serologic testing
  - Non-treponemal test (RPR, VDRL, ART)
  - Treponemal test (MHA-TP, FTA-ABS)
- Serologic testing for vaccine preventable diseases (if indicated—see text)
- Tuberculin skin test or Chest radiograph (see text)

Tuberculosis

The incidence of TB in Haiti is one of the highest in the Western hemisphere, at 306/100,000 for all forms of TB. By comparison, the US rate is 4.2 per 100,000 (source: Global Tuberculosis Control: epidemiology, strategy, financing: WHO report 2009 (PDF - 314 PAGES) .
Because of the high incidence of TB in Haiti, in addition to the living conditions of most orphans, all orphan parolees should be evaluated for TB disease after arrival. This evaluation should consist of medical history, physical examination, *and if adequate follow up can be guaranteed, screening orphans 2-14 years of age with the tuberculin skin test (TST) or interferon-gamma release assay (IGRA) is recommended.* Physicians should be advised that some experts prefer TST in children younger than 5 years of age. There are relatively few published reports documenting the performance of IGRAs in young children, obtaining sufficient blood is more difficult, and there is concern that IGRAs may perform differently in very young children who are at greater risk of a poor outcome if infection is undiagnosed. If the TST is ≥10 mm or IGRA is positive, a chest radiograph (CXR) (anteroposterior or posteroanterior view and a lateral view for applicants <10 years of age; posteroanterior view for applicants ≥10 years of age) should be performed.

If adequate follow-up cannot be guaranteed, the TST or IGRA can be omitted and a CXR can be done as the initial screening test.

The following categories of children should provide sputum specimens:

- Orphans with signs and symptoms of TB
- Medical history suggesting TB
- CXR findings suspicious of TB
- HIV infection

Three sputum specimens (or alternative specimens such as gastric aspirates if the child cannot provide sputum specimens) should be provided to undergo microscopy for acid-fast bacilli (AFB), as well as culture for mycobacteria and confirmation of the *Mycobacterium* species, at least to the *M. tuberculosis* complex level. Orphans diagnosed with TB disease should be started on treatment with treatment delivered as directly observed therapy (DOT).

For any child requiring sputum specimens to be sent, the medical provider should contact the local health department of the final placement location of the child, to ensure appropriate follow-up.

Once the orphans are in a long-term placement, those not diagnosed with TB disease and started on DOT, and without documented TST or IGRA results from their initial screening, should be evaluated for latent *M. tuberculosis* infection (LTBI). LTBI evaluation should consist of either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA). Orphans with a negative test for TB infection should have LTBI testing repeated 6 months after arrival.

Receipt of bacille Calmette-Guérin (BCG) vaccine is not a contraindication to a TST, and a positive TST result should not be attributed to BCG vaccine. A patient with a known positive TST should not have the skin test repeated as it may provoke a local reaction.

Elements of the medical history for TB should include:

- Previous history of TB
- Illness suggestive of TB (such as cough of >3 weeks duration, dyspnea, weight loss, fever, or hemoptysis)
- Prior treatment suggestive of TB treatment (especially if incomplete of discontinued)
- Prior diagnostic evaluation suggestive of TB

Children are less likely than adults to present with "classic" signs and symptoms of TB such as night sweats, hemoptysis or cavitary findings on chest x-ray. Children more frequently present with generalized findings such as fever, growth delay, and weight loss. Children are also more prone to extra-pulmonary TB, such as meningitis, and disease of the middle ear and mastoid, lymph nodes, bones, joints, and skin. Clinical symptoms can be subtle. The clinician should keep in mind that TB can present with virtually any sign or symptom and should be included in the differential diagnosis of most abnormal clinical findings.

Pertinent elements of the physical exam specific for TB include;

- Thorough pulmonary examination
- Inspection and palpation of appropriate lymph nodes
- Inspection for scars of scrofula, and prior chest surgery

Vaccine Preventable Diseases

Vaccine preventable diseases (VPD) are another important public health consideration for this population. Haiti provides BCG, diphtheria, pertussis (whooping cough) and tetanus (DTwP); measles rubella (MR); oral poliovirus (OPV); and tetanus and diphtheria toxoids (Td), as part of its routine immunization schedule (along with Vitamin A). However, vaccination coverage rates are low for most of these vaccines. For example in 2008, coverage for measles vaccination was 58%, third dose DTP 53%, and third dose polio 52%. Moreover, Haiti does not provide a second measles dose, hepatitis A, hepatitis B, *Haemophilus influenzae* type b (Hib), rubella, varicella, rotavirus, meningococcal, or pneumococcal vaccinations, which are considered routine childhood immunizations in the U.S.

Children and adolescents adopted from Haiti should receive immunizations according to the recommended schedule in the United States for healthy children and adolescents (PDF - 1 PAGE) .

In general, when data are available for the orphans in a country, written documentation of immunizations (if available) can be accepted as evidence of adequacy of previous immunization if the vaccines, dates of administration, number of doses, intervals between doses, and age of the child at the time of immunization, are consistent internally and comparable to current U.S. or World Health Organization schedules. *However, given the limited data available regarding verification of immunization records in Haitian orphans, and the known low vaccine coverage rates in Haiti, it may be preferred to re-immunize the child presumptively. It is also acceptable to perform serologic evaluation of concentrations of antibodies to vaccines for certain antigens (i.e. measles, mumps, rubella, hepatitis A, polio, tetanus and diphtheria) (CDC. General Recommendations on*

Immunization. MMWR 2006;55 (No. RR-15):[34]). Because the rate of more serious local reactions after diphtheria, tetanus, and pertussis (DTaP) vaccine increases with the number of doses administered, serologic testing for antibody to tetanus and diphtheria toxins before re-immunizing (or if a serious reaction occurs) can be considered if appropriate immunization is in question.

Serologic testing for the surface antigen of the hepatitis B virus (HBsAg) should be performed on all children to identify chronic infection. If serologic testing is not available and receipt of immunogenic vaccines cannot be ensured, the prudent course is to provide the immunization series.

Ideally, adoptive parents, family members and other close personal contacts should ensure they are immunized or otherwise immune to hepatitis A virus infection before international travel to pick up the child. If this is not feasible, serologic testing of the orphan for hepatitis A IgM and IgG is recommended, to identify current/recent or past infection. If a child has no evidence of previous infection, the child should be immunized against hepatitis A according to the recommended immunization schedule. If IgG tests positive, indicating past infection, no immunization will be required for the child. If IgM is positive, indicating current/recent infection, all close contacts and family members should be immunized. Orphans or their household or other close contacts with symptoms consistent with acute viral hepatitis should be evaluated promptly.

HIV

Screening for HIV should be performed on all orphans from Haiti. Transplacentally acquired maternal antibody in the absence of infection can be detected in a child younger than 18 months of age. Hence, positive HIV antibody test results in asymptomatic children of this age require clinical evaluation, further testing (follow-up serologic and PCR), and counseling.

Intestinal Parasites

In a nationwide survey on intestinal helminths in 5,792 urban and rural school children conducted in Haiti in 2002, 34% of stools tested positive for intestinal helminths with the following parasites identified: *Ascaris lumbricoides* (27.3%), *Trichuris trichiura* (7.3%), *Necator americanus* (3.8%), *Hymenolepsis nana* (2%), *Taenia sp*. (0.3%) and *Strongyloides stercoralis* (0.2%) (Champetier de Ribes et al, Bull Soc Pathol Exot. 2005 Jun; 98(2):127-32).

Most experts would perform three stools for ova and parasite (O&P) testing collected on three consecutive mornings on all children, regardless of symptoms. If stool O & P examinations are negative and the child has eosinophilia (absolute eosinophil count exceeding 450 cells/mm3), then strongyloides species serologic testing is recommended, as stool O&P have poor sensitivity for this infection and the disease can be chronic and lead to serious morbidity (Red Book®: 2009 Report of the Committee on Infectious Diseases - 28th Ed. 2009).

If gastrointestinal tract signs or symptoms are present, send stool specimens for culture, and stool antigen testing for giardia, cryptosporidia, and rotavirus.

Malaria

Over 99% of the malaria parasite species that cause malaria in Haiti are *P. falciparum*, where it is endemic. It has been reported that up to 75% of the population of Haiti lives in malarious areas, especially at altitudes <300 m above sea level (*Garcia-Martin,* Am J Trop Med Hyg. 1972; 21:617–33*). Therefore, it is recommended to screen symptomatic orphans for malaria with a malaria smear.* Treatment guidelines can be found on the CDC website (PDF 3 PAGES).

Syphilis

Clinicians should screen each orphan for syphilis by reliable nontreponemal and treponemal serologic tests. Children with positive treponemal serologic test results should be evaluated by someone with special expertise to assess the differential diagnosis of pinta, yaws, and syphilis and to determine extent of infection so appropriate treatment can be administered.

Mental Health

Because of stigma in Haitian culture around mental illness, many children may be reluctant to discuss or admit to mental health problems. Likewise, prior caregivers in Haiti may not have fully explored such issues, even prior to the earthquake. The experience of the January 2010 Haitian earthquake would be expected to impact greatly on many of the orphans exposed. Clinicians should consider potential mental health and developmental issues. When mental health referrals are warranted, added care should be made to explain and arrange such referrals to the patient and his or her caregivers in a culturally sensitive, supportive, and non-stigmatizing way.

Conclusion

This document presents recommendations for an immediate medical screening of Haitian orphans entering the U.S. under humanitarian parole status. This is not a comprehensive examination, and it is strongly recommended to have a comprehensive medical history and physical examination once they arrive at their final destination to evaluate other medical and developmental issues in the child. These include hearing and vision assessment, evaluation of growth and development, blood lead concentration, complete blood cell count with red blood cell indices, newborn screening and/or measurement of thyroid-stimulating hormone concentration and examination for congenital anomalies (including fetal alcohol syndrome). (Red Book®: 2009 Report of the Committee on Infectious Diseases - 28th Ed. 2009).

Questions should be directed to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, 866/628-9891, or 800/392-0272 (24/7).

Health Advisory:

Human Paragonimiasis Following Ingestion of Raw Crayfish from Rivers in Missouri

April 30, 2010

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Health Advisory
April 30, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Human Paragonimiasis Following Ingestion of Raw Crayfish from Rivers in Missouri**

The Missouri Department of Health and Senior Services (DHSS) is alerting medical providers about the occurrence of six confirmed and probable human paragonimiasis cases in Missouri. Three of these cases have been reported since October 2009. The most recent case was reported in early April 2010. Since human paragonimiasis is considered to be very rare in North America, six cases reported to Missouri DHSS in the past three years are alarming. All of these patients had ingested raw crayfish from rivers in Missouri.

Background:
Human paragonimiasis is a food-borne parasitic infection caused by the trematode *Paragonimus* (the lung fluke). Infection in humans mainly occurs by ingestion of raw or undercooked freshwater crabs or crayfishes. Paragonimiasis caused by *Paragonimus westermani* is common in East Asia where it is associated with ingestion of raw or marinated crabmeat. Rare cases of paragonimiasis have been reported in North America. North American cases are caused by *P. kellicotti*, a parasite that is common in crayfish in the central USA including Missouri.

Clinical presentation:
Paragonimiasis typically presents with fever, cough, and eosinophilia. Some patients have hemoptysis, and the clinical presentation can mimic tuberculosis. Pulmonary symptoms and fevers typically develop one or more months after ingestion of raw crabs or crayfish. The parasites sometimes migrate to ectopic locations such as subcutaneous tissue (presenting as migratory nodules) or even the central nervous system (with headache, seizures, or visual symptoms).

Patients with paragonimiasis often have abnormal chest exams with rales, rhonchi, or signs of pleural effusion. Eosinophilia is common (>5% eosinophils or absolute count >500). Most also have abnormal chest radiographic findings with focal infiltrates and/or pleural effusions. Bronchoalveolar lavage (BAL) and pleural fluid from patients with pulmonary paragonimias typically show increased eosinophils.

Diagnosis:
Clinical diagnosis requires awareness of the illness and a high index of suspicion. Patients with the triad of fever, cough, and eosinophilia should be asked about raw crayfish ingestion. In patients with consistent history and fever, cough, eosinophilia, and/or hemoptysis, diagnosis of paragonimiasis should be considered. Chest X-rays in such patients may show focal infiltrates and/or pleural effusions. The parasite can migrate to the CNS, and suspected cases with headaches, seizures, or visual symptoms should have CNS imaging studies performed. Parasitological diagnosis by detection of parasite eggs in sputum or stool is specific but insensitive. Serology can be useful to confirm a clinical diagnosis of paragonimiasis. The Centers for Disease Control and Prevention (CDC) performs an immunoblot assay that is highly sensitive (96%) and specific (99%) for *P. westermani*, the species native to Asia. However, the sensitivity of this test in patients with *P. kellicotti* has not been established due to rarity of this illness in North America.

Treatment:
Paragonimiasis is treated with praziquantel (25 mg/kg orally three times daily for two days). Although all of the Missouri patients required hospitalization, they all had excellent clinical responses to praziquantel with improved symptoms within days and resolution of eosinophilia over a period of weeks to months.

DHSS urges persons who develop fever, cough, or hemoptysis after ingestion of raw crabs or crayfish to seek medical care. Medical Providers who know of other proven or suspect cases are encouraged to report these cases to their local public health agency (LPHA), or to DHSS at 866-628-9891 or by fax at 573 526-0235. Dr. Philip Lo at DHSS, (Philip.Lo@dhss.mo.gov; (573) 526-1369) is available for consultation.

DHSS advises that crabs and crayfish should be thoroughly cooked prior to consumption to avoid the risk of paragonimiasis. DHSS has distributed posters to campgrounds and canoe rental businesses to warn the public about the danger of eating raw crayfish. Questions can be directed to the LPHA, or to DHSS' Bureau of Communicable Disease Control and Prevention at (573) 751-6113, or 866-628-9891.

Additional information at:

1. http://www.journals.uchicago.edu/doi/full/10.1086/605534
2. http://www.dpd.cdc.gov/dpdx/HTML/Paragonimiasis.htm
3. http://cmr.asm.org/cgi/content/abstract/22/3/415

Health Advisory:

Possible Dengue Infections Among Relief Workers Returning From Haiti

May 11, 2010

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Health Advisory
May 11, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Possible Dengue Infections Among Relief Workers Returning From Haiti**

On April 27, the Centers for Disease Control and Prevention (CDC) issued a Health Advisory entitled *Potential for Dengue Infection Among Relief Workers Returning from Haiti* (http://www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00312). The following includes information and recommendations from this CDC document, as well as additional guidance specific to Missouri health-care providers.

Purpose

To encourage health-care providers to consider dengue infection in the differential diagnosis of febrile illness in relief workers returning from Haiti and to submit diagnostic samples to the Missouri State Public Health Laboratory (MSPHL) or CDC for appropriate testing.

Target Audience

Medical providers evaluating any person who has recently been in Haiti, including critical care providers, primary care providers, infectious disease physicians, hospital infection control personnel, public health staff, and commercial diagnostic laboratory workers.

Background

The January 12, 2010, earthquake in Haiti caused extensive damage to homes and utilities and left many residents without proper shelter. Exposure to the elements has likely increased the risk of contact with mosquitoes that may spread diseases such as dengue. Since dengue is endemic in Haiti, the CDC Dengue Branch advises that physicians evaluate travelers returning with a febrile illness (or a recent history of febrile illness) from Haiti.

Potential Public Health Concerns

Because mosquitoes that transmit dengue are common in parts of the US, including Missouri, an infected traveler can touch off a localized dengue outbreak. Three states (Florida, Texas, and Hawaii) have had local outbreaks identified in the last decade.

Symptoms of Dengue Fever

Dengue fever (DF) is characterized by an acute high fever plus two or more of the following: headache, retro-orbital pain, joint pain, muscle or bone pain, rash, mild hemorrhagic manifestations (e.g., nose or gum bleed, petechiae, or easy bruising), and leukopenia. The incubation period for DF ranges from 3 to 14 days, but is typically about one week; therefore, illness can occur while workers are stationed in Haiti or after they return to the US. Most DF cases are self-limited and can be treated with bed rest, acetaminophen, and oral fluids.

Symptoms of Dengue Hemorrhagic Fever

A small proportion of patients develop dengue hemorrhagic fever (DHF), which is characterized by a fever lasting 2 to 7 days, any hemorrhagic manifestation, thrombocytopenia (platelet count <100,000/mm^3), and abnormal vascular permeability evidenced by hemoconcentration, hypoalbuminemia, or abdominal or pleural effusions. DHF can result in circulatory instability or shock, and the risk for these complications may be increased among persons with prior dengue infection. Adequate management of DHF patients generally requires timely hospitalization and judicious administration of intravascular fluids and close monitoring of vital signs and hemodynamic status. Physicians who suspect that a patient has DHF may wish to consult the CDC Dengue Branch at (787) 706-2399. A four-page clinical management tool can be downloaded from http://www.cdc.gov/dengue/resources/Dengue&DHF%20Information%20for%20Health%20Care%20Practitioners_2009.pdf.

Recommendations

- Physicians seeing a patient who has illness consistent with dengue and who has traveled to Haiti within the past 30 days should submit test specimens to a public health laboratory rather than a commercial laboratory.
  - MSPHL can facilitate specimen shipment to the CDC Dengue Branch through the MSPHL Courier Service for Specimen Transportation.
  - The CDC Dengue Branch provides free diagnostic testing for physicians, and confirmatory dengue testing for commercial laboratories.
- Initiation of supportive care should not be delayed pending results of laboratory testing. However, laboratory results can be used to inform primary prevention efforts within the patient's household and community.
- While some commercial laboratories in the US offer diagnostic services for dengue, commercial labs are not always able to provide results that can distinguish recent from past dengue infection.

Instructions for Obtaining and Submitting Samples

NOTE: Information received on each case (e.g. date of onset of symptoms, date of sample collection) is crucial in selecting and interpreting laboratory analyses. In addition, a complete address and travel history are critical for identifying areas where dengue surveillance, prevention, and control measures should be implemented.

- Whenever possible, physicians should submit paired acute and convalescent samples to facilitate optimal diagnostic testing. The following table summarizes the timing and type of specimen needed for dengue infection analysis:

Type of Sample	Interval Since Onset of Symptoms	Type of Analysis	Specimen Type
Acute	Until day 5	RT-PCR for dengue virus	Serum, 2ml, red-topped tube
Convalescent	6 to 30 days	ELISA for dengue IgM	Serum, 2 ml, red-topped tube

- Each specimen consists of 2 ml (cc) of centrifuged serum; freeze serum immediately after separation and ship on dry ice.

- All specimens must be accompanied by a completed Dengue Case Investigation Form (http://www.cdc.gov/Dengue/resources/caseformhaiti.pdf) with "Haiti Travel" printed on the heading of the form.

- Specimens and forms can be transported by either of two methods:

1. **Through the MSPHL Courier Service:**
   - MUST INCLUDE the CDC Dengue Case Investigation Form noted above (http://www.cdc.gov/Dengue/resources/caseformhaiti.pdf).
   - An additional Specimen Submission Form (CDC 50.34) is required for specimens transported via the MSPHL Courier Service: http://www.cdc.gov/ncidod/dvbid/misc/CDC50_34.pdf
   - Information on using the MSPHL Courier Service: http://www.dhss.mo.gov/Lab/CourierInformation.doc
   - Courier Pickup Locations: http://www.dhss.mo.gov/Lab/CourierPickupLocations.pdf
   - For more information: (573) 751-3334

OR

2. **Direct shipment to the CDC Dengue Branch:**

   - MUST INCLUDE the CDC Dengue Case Investigation Form noted above (http://www.cdc.gov/Dengue/resources/caseformhaiti.pdf).
   - Ship to: Centers for Disease Control and Prevention
     Dengue Branch
     1324 Cañada Street
     San Juan, Puerto Rico 00920
     Tel: (787) 706-2399; fax (787) 706-2496

Public Health Disease Reporting

- DF and DHF are reportable conditions in Missouri.
- By using the CDC Dengue Case Investigation Form, medical providers comply with Missouri's disease reporting requirement.
- Local public health agencies can assist in public health investigations and prevention of possible local dengue transmission.

For More Information

- Questions about this Health Advisory should be directed to DHSS's Office of Veterinary Public Health at (573) 526-4780.
- For questions about the MSPHL Courier Service, call (573) 751-3334.
- Detailed criteria for the processing of dengue samples at the CDC Dengue Branch are available at: http://www.cdc.gov/Dengue/resources/TestpolEng_2.pdf.
- Additional information about dengue is available at: http://www.cdc.gov/dengue/.
- CDC's toll-free information line, 800-CDC-INFO (800-232-4636), TTY: (888) 232-6348, is available 24 hours a day, every day.

Health Advisory:

Measles Cases Identified in Southwestern Missouri

May 12, 2010

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Advisory
May 12, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Measles Cases Identified in Southwestern Missouri**

On May 10, 2010, the Missouri Department of Health and Senior Services (DHSS) reported two laboratory-confirmed cases of measles among residents of southwestern Missouri. The two cases involved an adult and a child of the same family who had recently returned from a trip to Venezuela. The child had not received a measles vaccine, and the vaccination status of the adult has not been confirmed. Persons with measles are considered contagious from 1 to 2 days prior to onset of symptoms (about 4 days before rash onset) to 4 days after the appearance of the rash. Therefore, potential transmission of the measles virus to unknown susceptible persons may have occurred.

If any patient presents with signs/symptoms suggestive of measles, he/she should be immediately isolated and appropriately evaluated by a health care professional. This evaluation must include obtaining a serum specimen for measles serological testing. The specimen, or a portion of the specimen, should be sent to the Missouri State Public Health Laboratory for testing. In the first 72 hours after rash onset, up to 20 percent of tests for IgM may give false-negative results. Tests that are negative in the first 72 hours after rash onset should be repeated. Health care providers should not rule out the possibility of measles based on a history of documented or undocumented measles immunization.

Any individual suspected of having measles should be immediately reported to the Springfield/Greene County Health Department at 417/864-1658, or to DHSS at 800/392-0272 (24 hours a day - 7 days a week).

To prevent measles, children (and some adults) should be vaccinated with the measles, mumps, and rubella (MMR) vaccine. Two doses of this vaccine are needed for complete protection. Children should be given the first dose of MMR vaccine at 12 to 15 months of age. The second dose can be given 4 weeks later, but is usually given before the start of kindergarten at 4 to 6 years of age. The "Recommended Immunization Schedules" can be obtained from the Centers for Disease Control and Prevention's web site at: http://www.cdc.gov/vaccines/recs/schedules/default.htm.

The next page provides a summary of the clinical features of measles. Questions should be directed to the Springfield/Greene County Health Department at 417/864-1658, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866/628-9891.

Measles: Summary of Clinical Features

The **incubation period** of measles, from exposure to onset of prodrome, averages 10-12 days (range 7-18 days). From exposure to rash onset averages 14 days (range, 7-18 days, can be up to 21 days on rare occasions).

The **prodrome** lasts 2-4 days (range 1-7 days). It is characterized by fever, which increases in stepwise fashion, often peaking as high as 103°-105°F. This is followed by the onset of cough, coryza (runny nose), and/or conjunctivitis.

Koplik's spots, a rash (enanthem) present on mucous membranes, are considered to be pathognomonic for measles. They are seen from 1-2 days before until 1-2 days after the onset of the rash, and appear as punctuate blue-white spots on the bright red background of the buccal mucosa.

The measles **rash** is a maculopapular eruption that usually lasts 5-6 days. It begins at the hairline, then involves the face and upper neck. During the next 3 days, the rash gradually proceeds downward and outward, reaching the hands and feet. The maculopapular lesions are generally discrete, but may become confluent, particularly on the upper body. Initially, lesions blanch with fingertip pressure. By 3-4 days, most do not blanch with pressure. Fine desquamation occurs over more severely involved areas. The rash fades in the same order that it appears, from head to extremities.

Other symptoms of measles include anorexia, diarrhea (especially in infants), and generalized lymphadenopathy.

Approximately 30% of reported measles cases have one or more complications. Some of these complications can be severe, and potentially fatal. Death from measles has been reported in approximately 1-3 per 1,000 reported cases in the United States in recent years. As with other complications of measles, the risk of death is higher among young children and adults. Pneumonia accounts for about 60% of deaths. The most common causes of death are pneumonia in children and acute encephalitis in adults.

Measles transmission is primarily person to person via large respiratory droplets. Airborne transmission via aerosolized droplet nuclei has been documented in closed areas (e.g., office examination rooms) for up to 2 hours after a person with measles occupied the area.

Measles is highly communicable, with >90% secondary attack rates among susceptible contacts. Measles may be transmitted from 4 days prior to 4 days after rash onset. Maximum communicability occurs from onset of the prodrome through the first 3-4 days of the rash.

Health Advisory:

Pertussis Identified in Two North-Central Missouri Amish Communities

July 12, 2010

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Health Advisory
July 12, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Pertussis Identified in Two North-Central Missouri Amish Communities**

The Missouri Department of Health and Senior Services (DHSS) would like to alert health care providers about a recent increase in reported pertussis cases in two Amish communities. Local public health officials identified pertussis outbreaks in two Schuyler County Amish communities during the past two weeks. At the time of this report (7/9/10), a total of three laboratory-confirmed and fourteen suspected cases had been identified in the two Schuyler County communities. Three of the cases were hospitalized, all of whom were children (one is less than six months of age). Pertussis immunization coverage among children and adults is low in both communities. Additionally, a pertussis outbreak was reported last month in a Morgan County Mennonite group.

While statewide incidence of pertussis is not currently in excess of the five-year median, pertussis cases have been reported in all regions of Missouri over the past month (82 total), 25% of whom were less than one year of age. Among these reports, a school-associated outbreak and a large household cluster were identified in Howell and Boone Counties, respectively.

The purpose of this DHSS Health Advisory is to: 1) increase awareness among medical providers that pertussis is circulating among Amish groups in northern Missouri as well as other parts of the state's general population, and 2) to review current diagnostic, treatment, prophylaxis, and prevention recommendations.

Clinical Manifestations

Pertussis is highly communicable and can cause severe disease or death in very young children. It begins with mild upper respiratory tract symptoms and progresses to cough. The condition can further progress to severe paroxysms, often with a characteristic inspiratory whoop followed by vomiting. Fever is absent or minimal. Among older children and adults, the disease usually results in symptoms that can be mistaken for bronchitis and URI's-persistent cough, but no whoop. In infants younger than six months, apnea is a common manifestation and the whoop may be absent. It is important to remember that while pertussis is most often considered a disease that affects young children, it can occur at any age. Pertussis should be considered in older children and adults who have a persistent cough lasting more than 7-14 days, which cannot be attributed to another specific illness. If untreated, these older children and adults can act as a reservoir for pertussis and infect younger children.

Diagnostic Testing

The only pertussis diagnostic tests endorsed by the Centers for Disease Control and Prevention (CDC) are culture and polymerase chain reaction (PCR). The CDC guidelines for laboratory confirmation of pertussis do not include serologic testing, as serology assays using commercial reagents are not validated clinically and do not differentiate between recent and past infection, and vaccination. Obtaining a positive culture result from a person with pertussis can be affected by several factors, such as how the specimen is handled, the

stage of illness at the time of specimen collection, the use of antimicrobial therapy prior to culture, immunity from past infection or from vaccination, and age of the case-patient. Several studies have shown that specimens obtained for culture are more likely to be positive within three weeks of cough onset. The PCR test could be positive beyond the three-week period. If a case patient is symptomatic in the absence of another cause and is a close contact of a confirmed pertussis case, DHSS does not recommend testing before treating the case-patient. Pertussis test kits, including swabs and transport media, can be obtained from local public health agencies (LPHAs) or the Missouri State Public Health Laboratory (573-751-3334).

Treatment

Specific treatment recommendations are available in the American Academy of Pediatrics *Red Book* (see references below). The *Red Book* and CDC recommend erythromycin as well as the new macrolides, clarithromycin or azithromycin dehydrate, as the antimicrobial agents for treatment or prophylaxis against pertussis. A possible alternative for patients who do not tolerate erythromycin is trimethoprim-sulfamethoxazole (TMP-SMZ). Once into the paroxysmal stage, antibiotics will not ameliorate the disease but will limit the spread to others. If appropriate antimicrobial therapy is contraindicated or the patient refuses treatment, the patient should be isolated until three weeks after the onset of paroxysms. LPHAs can provide epidemiological consultation when required.

Prophylaxis of Household and Other Close Contacts

Chemoprophylaxis is recommended for all household and other close contacts regardless of age, whether the contact has pertussis-like symptoms, or immunization status. Close contacts are defined as those persons having direct contact with respiratory, oral, or nasal secretions from a symptomatic case-patient; having direct face-to-face contact, regardless of duration, with a symptomatic case; or having shared a confined space in close proximity for a prolonged period of time with a symptomatic case.

Immunization

The best way to reduce the incidence of pertussis is to have a highly vaccinated population. This should be accomplished through physicians' offices and public health clinics. Close contacts under the age of seven years who are unimmunized or underimmunized should have pertussis immunization initiated or continued according to the recommended schedule. Children who received their third dose six months or more before exposure should be given a fourth dose at this time as a protective measure. Children who received their fourth dose three or more years before exposure and who are younger than seven years of age should be given a fifth dose of DTaP at this time. A booster Tdap vaccine should be given to people 11-18 years of age if they have not previously received Tdap. Adults 19-64 years of age should receive a single dose of Tdap if it has been more than two years since their last Td vaccine, and they have not previously received Tdap. Shorter intervals can be considered if necessary.

In households with infant(s) less than twelve months of age, all children in the household should be up-to-date with the recommended doses of DTaP and all adults (including the mother) and adolescent household contacts should be appropriately vaccinated with a dose of Tdap, if they have not previously received Tdap.

Reporting

Health care providers are also requested to assist in the control of pertussis through immediate reporting of suspect cases by telephone to their LPHA, or to DHSS (800-392-0272).

References

1. Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine - Preventable Diseases*. Atkinson W, Wolfe S, Hamborsky J, McIntyre L, eds. "Pertussis." 11th Ed. Washington DC: Public Health Foundation, 2009, 199 – 216.
(Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm)

2. Centers for Disease Control and Prevention. Prevention of Pertussis, Diptheria and Tetanus among Pregnant and Postpartum Women and their Infants. *Morbidity and Mortality Weekly Report*, 2008;57(No.RR-4).
(Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5704a1.htm)

3. Academy of Pediatrics. "Pertussis". In: Pickering L, ed. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 27th Ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: 504 – 519.

DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine

Tdap = tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine

Td = tetanus and diphtheria toxoids vaccine

Health Advisory:

Increased Potential for Dengue Infection in Travelers Returning from International and Selected Domestic Areas

July 23, 2010

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Advisory
July 23, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Increased Potential for Dengue Infection in Travelers Returning from International and Selected Domestic Areas**

On July 22, 2010, the Centers for Disease Control and Prevention (CDC) issued a Health Advisory entitled "Increased Potential for Dengue Infection in Travelers Returning from International and Selected Domestic Areas." Pertinent sections of this document are reproduced below along with additional information for Missouri healthcare providers.

Summary

Dengue virus transmission has been increasing to epidemic levels in many parts of the tropics and subtropics. Travelers to these areas are at risk of acquiring dengue virus and developing dengue fever (DF) or the severe form of the disease, dengue hemorrhagic fever (DHF). CDC, and the Missouri Department of Health and Senior Services (DHSS), strongly advise that health care providers should: 1) consider DF and DHF when evaluating patients returning from dengue-affected areas--both domestic and abroad--who present with an acute febrile illness within two weeks of their return, 2) submit serum specimens for appropriate laboratory testing as described below, and 3) report all presumptive and confirmed cases of DF and DHF to their local public health agency (LPHA), or to DHSS at 573/751-6113 or 800/392-0272 (24/7).

Background

Dengue transmission has been increasing to epidemic levels in many parts of the tropics and subtropics where it had previously been absent or mild. Dengue-affected areas are widely distributed throughout Africa, Asia, Pacific, the Americas and the Caribbean. This calendar year, more than 50 countries have reported evidence of dengue transmission; including 17 countries in Asia, 17 in the Americas, 10 in Africa, seven in the Caribbean, and one in the Pacific. With an extensive dengue outbreak occurring in Puerto Rico and evidence of continued transmission in Key West, Florida, travel to certain domestic locations may also pose a risk for the traveler. The mosquitoes known to transmit dengue virus, *Aedes aegypti* and *Aedes albopictus*, are present throughout much of the southeastern United States and infected returning travelers may pose a risk for initiating local transmission.

Symptoms

Dengue virus infections can manifest as a subclinical infection or DF, and may develop into potentially fatal DHF. DF is a self-limited febrile illness that is characterized by high fever plus two or more of the following: headache, retro-orbital pain, joint pain, muscle or bone pain, rash, mild hemorrhagic manifestations (e.g., bleeding of nose or gums, petechiae, or easy bruising), and leukopenia. Because the incubation period for dengue infection ranges from 3 to 14 days, the patient may not present with illness until after returning from travel. Clinical management of DF consists of symptomatic treatment (avoid aspirin, NSAIDS and corticosteroids, as they can promote hemorrhage) and monitoring for

the development of severe disease at or around the time of defervescence. A small proportion of patients develop DHF, which is characterized by presence of resolving fever or a recent history of fever, lasting 2–7 days, any hemorrhagic manifestation, thrombocytopenia (platelet count $\leq$100,000/mm^3), and increased vascular permeability, evidenced by hemoconcentration, hypoalbuminemia or hypoproteinemia, ascites, or pleural effusion. DHF can result in circulatory instability or shock. Adequate management requires timely recognition and hospitalization, close monitoring of hemodynamic status, and judicious administration of intravascular fluids. There is no antiviral drug or vaccine against the dengue virus. Updated guidelines for the management of dengue can be found at http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf.

Recommendations

- Health care providers seeing patients with dengue-like illness who have recently traveled to Puerto Rico, Key West, Florida, or international dengue-affected areas (see world distribution of dengue maps at http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/dengue-fever-dengue-hemorrhagic-fever.aspx) should report cases to their LPHA or to DHSS, and send specimens for laboratory testing. DF and DHF are now nationally notifiable conditions in the United States. Please remember that apart from individuals traveling for tourism, individuals responding to international disasters (e.g., Haiti earthquake), participating in medical or religious missionary work, and visiting friends and relatives are often returning from dengue-affected areas and should be evaluated for dengue infection if they present with dengue-like illness during or after their travel.

- Reporting to local public health officials and consideration of hospitalization to initiate supportive care should not be delayed pending test results. Reporting suspected dengue cases will trigger a public health investigation and the implementation of prevention measures. **Report cases to your LPHA (contact information for all LPHAs can be found at:** http://www.dhss.mo.gov/LPHA/PublicHealthAgencies.html**), or to DHSS' Bureau of Communicable Disease Control and Prevention at 573/751-6113 or 800/392-0272 (24/7).**

- Specimens from patients with acute febrile illness who returned from dengue-affected areas within the past 14 days should be submitted for testing.

- Specimens for dengue testing may be sent to the Missouri State Public Health Laboratory (MSPHL) Virology Unit, where they will then be forwarded to CDC for testing. **Please contact MSPHL for shipping instructions at 573-751-3334.** Instructions for sample processing can be found at http://www.cdc.gov/Dengue/resources/TestpolEng_2.pdf. A completed CDC Dengue Case Investigation Form must accompany the specimens for the appropriate testing to be performed. This form is found at http://www.cdc.gov/Dengue/resources/DCIF_English_ColorSept1508_FINAL_.pdf.

- Healthcare providers may also submit specimens directly to the CDC laboratory in San Juan, Puerto Rico.

  Centers for Disease Control and Prevention
  Dengue Branch
  1324 Cañada Street
  San Juan, Puerto Rico 00920
  Tel: 787/706-2399; Fax: 787/706-2496

  CDC offers free diagnostic testing for health care providers and confirmatory dengue testing for health department and private laboratories.

  Instructions for preparing and delivering specimens for dengue testing to the CDC Dengue Branch are available at www.cdc.gov/Dengue/resources/TestpolEng_2.pdf. A completed CDC Dengue Case Investigation Form must accompany the specimens for the appropriate testing to be performed. This form is found at http://www.cdc.gov/Dengue/resources/DCIF_English_ColorSept1508_FINAL_.pdf.

- Whenever possible, submit paired acute and convalescent specimens (2 ml of centrifuged serum.) Accuracy is increased when both acute and convalescent specimens are available for testing. But providers should not wait and should submit acute specimens as soon as available; a convalescent specimen can be submitted when available.

Type of specimen	Interval since onset of symptoms	Type of Analysis
Acute	until day 5	RT-PCR for dengue virus
Convalescent	6 to 30 days	ELISA for dengue IgM

For More Information

- Questions should be directed to DHSS' Office of Veterinary Public Health at 573/751-6113.
- Additional information about dengue is available at: www.cdc.gov/dengue.
- CDC has a toll-free information line, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, available 24/7.

Health Advisory:

Cryptosporidiosis Identified in the Greater Metropolitan St. Louis Area

August 6, 2010

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Health Advisory
August 6, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Cryptosporidiosis Identified in the Greater Metropolitan St. Louis Area**

The Missouri Department of Health and Senior Services (DHSS) would like to alert health care providers about a recent increase in reported cryptosporidiosis cases in the greater metropolitan St. Louis area. Local public health officials have identified cryptosporidiosis outbreaks associated with two area swimming pools. Officials in Illinois and Missouri are currently investigating illnesses in four groups of persons who were at these swimming pools. Attack rates among members of these groups have been as high as 100% in swimmers <30 years old.

The purpose of this DHSS Health Advisory is to: 1) increase awareness among medical providers that cryptosporidiosis has been associated with swimming pools in the greater St. Louis area, and 2) to review current diagnostic, treatment, and prevention recommendations.

Clinical Manifestations

Cryptosporidium is a parasite found in the intestine of infected humans and animals. Transmission is via the fecal-oral route, which includes person-to-person, animal-to-person, waterborne, and foodborne transmission. Frequent non-bloody, watery diarrhea; vomiting; and low-grade fever are the most common manifestations of cryptosporidiosis. Other symptoms/signs include stomach cramps, nausea, fatigue, loss of appetite, and weight loss. Illness usually lasts from 1 to 20 days (mean is 10 days). Infected persons may have mild symptoms or may be asymptomatic. In persons with weakened immune systems, *Cryptosporidium* infection can result in very serious illness, and even death.

Incubation period ranges from 2 to 14 days, and is usually about 7 days.

As long as *Cryptosporidium* is present in the stool, a person can transmit the parasite to others. In most persons, shedding of *Cryptosporidium* ends within 2 weeks.

Diagnostic Testing

Unfortunately, routine laboratory examination of stool for ova and parasites may not detect *Cryptosporidium* species. The formalin ethyl acetate stool concentration method is recommended before staining stool with a modified Kinyoun acid-fast stain. Direct immunofluorescent assay (DFA) for detection of oocysts in stool, and enzyme immunoassay (EIA) for detecting antigen in stool, are available commercially. The DFA is considered the "Gold Standard" of diagnostic testing, and is routinely performed by the Missouri State Public Health Laboratory (MSPHL) on all stools sent in for parasite examination. With EIA methods, false-positive and false-negative results can occur, and confirmation by microscopy should be considered. Because shedding can be intermittent, at least 3 stool specimens collected on separate days should be examined before considering test results to be negative. Oocysts are small (4–6 µm in diameter) and can be missed in a rapid scan of a slide. Organisms also can be identified in intestinal biopsy tissue or intestinal fluid. Polymerase chain reaction (PCR) assays are used to identify species and genotype.

MSPHL does *Cryptosporidium* testing on stool as part of its routine intestinal parasite exam. MSPHL can also provide stool collection kits and instructions. For more information, including contact information, go to MSPHL's Web site at http://www.dhss.mo.gov/Lab/Microbiology/Parasitology.html.

Treatment

Specific treatment recommendations are available in the American Academy of Pediatrics' *Red Book*. The 2009 *Red Book* provides the following: Generally, immunocompetent people need no specific therapy. A 3-day course of nitazoxanide oral suspension has been approved by the US Food and Drug Administration for treatment of immunocompetent children beginning at 12 months of age and adults with diarrhea associated with cryptosporidiosis. Patients with acquired immunodeficiency syndrome with immune reconstitution resulting from highly active antiretroviral therapy frequently will have clearance of *Cryptosporidium* organisms. Paromomycin, alone or with azithromycin, is minimally effective. In immunocompromised patients with cryptosporidiosis, oral administration of human Immune Globulin Intravenous or bovine colostrum has been beneficial. In HIV-infected patients, antiretroviral therapy-associated improvement in CD4+ T-lymphocyte count can improve the course of disease.

Nitazoxanide (Alinia) significantly shortens the duration of diarrhea. Also, lactose intolerance is common in cryptosporidiosis, and lactose-containing foods should be avoided.

Reporting

Health care providers are requested to assist in the control of cryptosporidiosis through immediate reporting of suspect cases by telephone to their local public health agency, or to DHSS at 800-392-0272.

Additional Information

For more information, contact DHSS' Bureau of Communicable Disease Control and Prevention at 573-751-6113 or 866-628-9891 (8-5 Monday through Friday), or call your local public health agency. See also the Centers for Disease Control and Prevention's (CDC's) cryptosporidiosis Web site at http://www.cdc.gov/crypto/**.**

Information for Patients

To reduce the risk of diseases such as cryptosporidiosis when swimming:

- Refrain from swimming when you have diarrhea.
- Avoid swallowing pool water or even getting it in your mouth.
- Shower before swimming and wash your hands after using the toilet or changing diapers. Your child may need help with handwashing.
- Take children on bathroom breaks or check diapers often.
- Change diapers in a bathroom and not at poolside and thoroughly clean the diaper changing area.
- Avoid putting water toys in mouth.

Facts About Crypto and Swimming Pools (CDC)
http://www.cdc.gov/healthywater/pdf/swimming/resources/cryptosporidium-factsheet.pdf

Additional information for the general public on cryptosporidiosis is available at:
http://www.cdc.gov/crypto/gen_info/index.html

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Academy of Pediatrics. "Cryptosporidiosis". In: Pickering L, ed. *Red Book: 2009 Report of the Committee on Infectious Diseases. 27th Ed*. Elk Grove Village, IL: American Academy of Pediatrics; 2009: 272-3.

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http://archpedi.ama-assn.org/cgi/content/full/161/9/878

Health Advisory:

Identification of *Enterobacteriaceae* Isolates Carrying a Newly Described Resistance Mechanism, the New Delhi Metallo-Beta-Lactamase (NDM-1)

September 8, 2010

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Health Advisory
September 8, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Identification of *Enterobacteriaceae* Isolates Carrying a Newly Described Resistance Mechanism, the New Delhi Metallo-Beta-Lactamase (NDM-1)**

This Health Advisory provides information on the identification of *Enterobacteriaceae* carrying a newly described resistance mechanism, the New Delhi metallo-beta-lactamase (NDM-1). Healthcare providers should be aware of the existence of this form of antibiotic resistance, monitor for its occurrence, use proper infection control guidelines to prevent further transmission, and use antibiotics appropriately to prevent further development of resistance.

On June 25, 2010, the Centers for Disease Control and Prevention (CDC) reported that during January-June 2010, three *Enterobacteriaceae* isolates carrying a newly described resistance mechanism, the New Delhi metallo-beta-lactamase (NDM-1), were identified from three states at the CDC antimicrobial susceptibility laboratory (*MMWR* 2010; 59[24]:750). This was the first report of NDM-1 in the U.S., and the first report of metallo-beta-lactamase (MBL) carriage among *Enterobacteriaceae* in the U.S.. These isolates, which include an *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae*, carry $bla_{\text{NDM-1}}$, which confers resistance to all beta-lactam agents except aztreonam (a monobactam antimicrobial); all three isolates were aztreonam resistant, presumably by a different mechanism.

Carbapenem resistance and carbapenemase production conferred by $bla_{\text{NDM-1}}$ is detected reliably with phenotypic testing methods currently recommended by the Clinical and Laboratory Standards Institute, including disk diffusion testing and the modified Hodge test. Carbapenem resistance in all three of the NDM-1 isolates was detected in the course of routine testing.

In the United Kingdom, where these organisms are increasingly common, carriage of *Enterobacteriaceae* containing $bla_{\text{NDM-1}}$ has been closely linked to receipt of medical care in India and Pakistan. All three U.S. isolates were from patients who received recent medical care in India.

(On September 2, 2010, CDC reported four additional MBL-producing strains of *Klebsiella* spp. from two states that contain non-NDM1 resistance genes.)

Like the *K. pneumoniae* carbapenemase (KPC)-producing strains of *Enterobacteriaceae* that are common in parts of the U.S., MBL-producing strains are usually resistant to most commonly used antimicrobials, including the carbapenems. Given the importance of *Enterobacteriaceae* in healthcare-associated infections and the extensive antimicrobial resistance found in these strains, carbapenem-resistant *Enterobacteriaeae* (CRE) are an important public health problem. In addition, as *Enterobacteriaceae* are a normal part of human flora, the potential for community-associated CRE infections also exists.

At the same time, it is important to keep in perspective the discovery of this small number of NDM-1 isolates in the U.S. Carbapenem resistance has been a problem in this country for about a decade, and NDM-1 is not the most common mechanism, only the newest. Certain other forms of antibiotic resistance, such as that associated with KPC-producing strains, are currently more problematic than that caused by NDM-1. Also, while resistance

conferred by NDM-1 (or KPC) makes infections much harder to treat, it does not, by itself, make the infecting organisms more virulent or transmissible. And, very importantly, all forms of antimicrobial resistance should be controllable through proper infection prevention measures and the judicious use of antibiotics. It must always be stressed that the overuse and misuse of antibiotics will create an environment in which microorganisms become resistant.

Current infection control guidance has been issued by CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC) for CRE (including NDM-1-producing isolates, as well as isolates with a different mechanism of resistance). This guidance emphasizes the importance of recognizing CRE when cultured from clinical specimens, placing patients colonized or infected with these isolates in contact precautions, and in some circumstances, conducting point prevalence surveys or active-surveillance testing among other high-risk patients. Laboratory identification of the carbapenem-resistance mechanism is not necessary to guide treatment or infection control practices, but should instead be used for surveillance and epidemiologic purposes. The complete guidance is available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5810a4.htm; healthcare facilities should ensure that these recommendations are properly implemented.

Clinicians should be aware of the possibility of NDM-1-producing *Enterobacteriaceae* in patients who have received medical care in India and Pakistan, and should specifically inquire about this risk factor when CRE are identified. CDC asks that carbapenem-resistant isolates from patients who have received medical care within 6 months in India or Pakistan be forwarded through state public health laboratories to CDC for further characterization.

Local public health officials should encourage healthcare facilities that identify CRE to follow the CDC/ HICPAC guidance for the control of these organisms.

Questions can be directed to Eddie Hedrick at the Missouri Department of Health and Senior Services' Bureau of Communicable Disease Control at 573/882-9881.

General questions about CRE can also be sent by email to cdcinfo@cdc.gov. In addition, questions from public health officials about the appropriate assessment and public health response to CRE in a given jurisdiction, and infection prevention practices to prevent transmission of these organisms, can be sent to CDC's Division of Healthcare Quality Promotion at hip@cdc.gov.

Reference

CDC. Detection of *Enterobacteriaceae* isolates carrying metallo-beta-lactamase — United States, 2010. *MMWR* 2010; 59(24):750.

Health Advisory:

Increase in Syphilis Cases in the St. Louis Area

October 26, 2010

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Health Advisory
October 26, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Increase in Syphilis Cases in the St. Louis Area**

The Missouri Department of Health and Senior Services (DHSS) is alerting medical providers to **an increase in syphilis cases in the St. Louis area among men who have sex with men (MSM); more than half of these cases are co-infected with human immunodeficiency virus (HIV)**.

Based on provisional data, from January 1 through September 28, 2010, there were 70 primary and secondary (P&S) syphilis cases reported from the St. Louis area, all were male. Of these 70 P&S cases, 59 (84.3%) were self-identified MSM. In addition, 40 (57.1%) of the 70 cases were co-infected with HIV. By comparison, during the same time period in 2009, there were a total of 50 P&S syphilis cases reported from the St. Louis area; 45 (90.0%) of these cases were in males, and 23 (46.0%) of the 50 cases were co-infected with HIV.

Interviews conducted by Disease Intervention Specialists on the 2010 cases indicated that among the HIV-positive men reported with P&S syphilis in St. Louis City, 69% had at least one HIV-positive partner; and that among the HIV-positive men reported with P&S syphilis in St. Louis County, 46% had at least one HIV-positive partner.

Current DHSS recommendations for medical providers are the following:

1. **All HIV-infected MSM, regardless of their area of residence, should be screened for syphilis at least every 6 months.**
2. **In addition, in the St. Louis area, all HIV-negative and HIV-status unknown MSM whose sexual behaviors put them at higher risk for sexually transmitted diseases (STDs) should be screened for syphilis at least every 6 months**. Such behaviors include, but are not limited to, multiple sexual partners, a new sexual partner, trading sex for money and/or drugs, anonymous sex, having a history of a bacterial STD, or having a sexual partner who engages in high risk behaviors.

Public Health testing locations can be found at http://www.takethetest.info/.

Reporting

Missouri law requires health care providers to report all known or suspected syphilis cases to public health officials within 24 hours. Reporting should preferably be done immediately by telephone to 573/526-5271, or 800/392-0272 (24/7). Disease case reports (using a CD-1 form) can be faxed to (573) 751-6417.

Missouri law also requires laboratories to report all reactive syphilis test results within 24 hours.

Missouri's Communicable Disease Reporting Rule (19 CSR 20-20.020) can be found at: http://www.sos.mo.gov/adrules/csr/current/19csr/19c20-20.pdf .

Questions can be addressed to DHSS' Bureau of HIV, STD, and Hepatitis at (573) 751-6439.

Educational opportunity for medical providers: The St. Louis STD/HIV Prevention Training Center will provide a Syphilis Update course at Washington University Medical Center on November 2, 2010. For more information about this course and to register visit their website at http://std.wustl.edu.

STD Treatment Guidelines from the Centers for Disease Control and Prevention (CDC)

The following are selected sections of CDC's 2006 Sexually Transmitted Diseases Treatment Guidelines, available at http://www.cdc.gov/std/treatment/2006/rr5511.pdf. See the full document for additional information on treatment of syphilis, including guidance for managing children and pregnant women, persons with penicillin allergy, and infants with congenital syphilis. (Note that these guidelines are currently being updated. When the new version becomes available, it can be accessed at http://www.cdc.gov/std/treatment/default.htm.)

Syphilis

General Principles

Background

Syphilis is a systemic disease caused by *Treponema pallidum*. Patients who have syphilis might seek treatment for signs or symptoms of primary infection (i.e., ulcer or chancre at the infection site), secondary infection (i.e., manifestations that include, but are not limited to, skin rash, mucocutaneous lesions, and lymphadenopathy), or tertiary infection (e.g., cardiac or ophthalmic manifestations, auditory abnormalities, or gummatous lesions). Latent infections (i.e., those lacking clinical manifestations) are detected by serologic testing. Latent syphilis acquired within the preceding year is referred to as early latent syphilis; all other cases of latent syphilis are either late latent syphilis or latent syphilis of unknown duration. Treatment for both late latent syphilis and tertiary syphilis theoretically might require a longer duration of therapy because organisms are dividing more slowly; however, the validity of this concept has not been assessed.

Diagnostic Considerations and Use of Serologic Tests

Darkfield examinations and direct fluorescent antibody (DFA) tests of lesion exudate or tissue are the definitive methods for diagnosing early syphilis. A presumptive diagnosis is possible with the use of two types of serologic tests: 1) nontreponemal tests (e.g., Venereal Disease Research Laboratory [VDRL] and RPR) and 2) treponemal tests (e.g., fluorescent treponemal antibody absorbed [FTA-ABS] and *T. pallidum* particle agglutination [TP-PA]). The use of only one type of serologic test is insufficient for diagnosis because false-positive nontreponemal test results are sometimes associated with various medical conditions unrelated to syphilis.

Nontreponemal test antibody titers usually correlate with disease activity, and results should be reported quantitatively. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:16–1:4 or from 1:8–1:32), is considered necessary to demonstrate a clinically significant difference between two nontreponemal test results that were obtained using the same serologic test. Sequential serologic tests in individual patients should be performed by using the same testing method (e.g., VDRL or RPR), preferably by the same laboratory. The VDRL and RPR are equally valid assays, but quantitative results from the two tests cannot be compared directly because RPR titers frequently are slightly higher than VDRL titers. Nontreponemal tests usually become nonreactive with time after treatment; however, in some patients, nontreponemal antibodies can persist at a low titer for a long period of time, sometimes for the life of the patient. This response is referred to as the serofast reaction.

The majority of patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of treatment or disease activity. However, 15%–25% of patients treated during the primary stage revert to being serologically nonreactive after 2–3 years. Treponemal test antibody titers do not correlate with disease activity and should not be used to assess treatment response.

Some clinical laboratories and blood banks have begun to screen samples using treponemal EIA tests. This strategy will identify both persons with previous treatment and persons with untreated or incompletely treated syphilis. False-positive results can occur, particularly among populations with a low prevalence of syphilis.

Persons with a positive treponemal screening test should have a standard nontreponemal test with titer to guide patient management decisions. If the nontreponemal test is negative, then a different treponemal test should be performed to confirm the results of the initial test. If a second trepomenal test is positive, treatment decisions should be discussed in consultation with a specialist. Some HIV-infected patients can have atypical serologic test results (i.e., unusually high, unusually low, or fluctuating titers). For such patients, when serologic tests do not correspond with clinical syndromes suggestive of early syphilis, use of other tests (e.g., biopsy and direct microscopy) should be considered. However, for the majority of HIV-infected patients, serologic tests are accurate and reliable for the diagnosis of syphilis and for following the response to treatment.

No single test can be used to diagnose neurosyphilis. The VDRL-cerebrospinal fluid (CSF) is highly specific, but it is insensitive. The majority of other tests are both insensitive and nonspecific and must be interpreted in relation to other test results and the clinical assessment. Therefore, the diagnosis of neurosyphilis usually depends on various combinations of reactive serologic test results, CSF cell count or protein, or a reactive VDRL-CSF with or without clinical manifestations. The CSF leukocyte count usually is elevated (>5 white blood cell count [WBC]/mm^3) in patients with neurosyphilis; this count also is a sensitive measure of the effectiveness of therapy. The VDRL-CSF is the standard serologic test for CSF, and when reactive in the absence of substantial contamination of CSF with blood, it is considered diagnostic of neurosyphilis. However, the VDRL-CSF

might be nonreactive even when neurosyphilis is present. Some specialists recommend performing an FTA-ABS test on CSF. The CSF FTA-ABS is less specific (i.e., yields more false-positive results) for neurosyphilis than the VDRL-CSF, but the test is highly sensitive. Therefore, some specialists believe that a negative CSF FTA-ABS test excludes neurosyphilis.

Management of Sex Partners

Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection. However, persons exposed sexually to a patient who has syphilis in any stage should be evaluated clinically and serologically and treated with a recommended regimen, according to the following recommendations:

- Persons who were exposed within the 90 days preceding the diagnosis of primary, secondary, or early latent syphilis in a sex partner might be infected even if seronegative; therefore, such persons should be treated presumptively.

- Persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.

- For purposes of partner notification and presumptive treatment of exposed sex partners, patients with syphilis of unknown duration who have high nontreponemal serologic test titers (i.e., ≥1:32) can be assumed to have early syphilis. However, serologic titers should not be used to differentiate early from late latent syphilis for the purpose of determining treatment.

- Long-term sex partners of patients who have latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation findings.

For identification of at-risk sexual partners, the periods before treatment are 1) 3 months plus duration of symptoms for primary syphilis, 2) 6 months plus duration of symptoms for secondary syphilis, and 3) 1 year for early latent syphilis.

DHSS' STD Disease Intervention Specialists (DIS) will provide assistance in confidential partner elicitation, notification, and referral for appropriate evaluation and treatment. For more information about DIS, contact Larry Phelan at (314) 877-2835.

Primary and Secondary Syphilis

Treatment

Recommended Regimen for Adults*

Benzathine penicillin G 2.4 million units IM in a single dose

* Recommendations for treating HIV-infected persons and pregnant women for syphilis have been discussed in this report (see Syphilis, Special considerations and Syphilis in Pregnancy).

Other Management Considerations

All patients who have syphilis should be tested for HIV infection. In geographic areas in which the prevalence of HIV is high, patients who have primary syphilis should be retested for HIV after 3 months if the first HIV test result was negative.

Patients who have syphilis and symptoms or signs suggesting neurologic disease (e.g., meningitis) or ophthalmic disease (e.g., uveitis, iritis, neuroretinitis, or optic neuritis) should have an evaluation that includes CSF analysis and ocular slit-lamp examination. Treatment should be guided by the results of this evaluation.

Invasion of CSF by *T. pallidum* accompanied by CSF abnormalities is common among adults who have primary or secondary syphilis. However, neurosyphilis develops in only a limited number of patients after treatment with the penicillin regimens recommended for primary and secondary syphilis. Therefore, unless clinical signs or symptoms of neurologic or ophthalmic involvement are present, CSF analysis is not recommended for routine evaluation of patients who have primary or secondary syphilis.

Follow-Up

Treatment failure can occur with any regimen. However, assessing response to treatment frequently is difficult, and definitive criteria for cure or failure have not been established. Nontreponemal test titers might decline more slowly for persons who previously had syphilis. Patients should be reexamined clinically and serologically 6 months and 12 months after treatment; more frequent evaluation might be prudent if follow-up is uncertain.

Patients who have signs or symptoms that persist or recur or who have a sustained fourfold increase in nontreponemal test titer (i.e., compared with the maximum or baseline titer at the time of treatment) probably failed treatment or were reinfected. These patients should be retreated and reevaluated for HIV infection. Because treatment failure usually cannot be reliably distinguished from reinfection with *T. pallidum*, a CSF analysis also should be performed. Clinical trial data have demonstrated that 15% of patients with early syphilis treated with the recommended therapy will not achieve a two dilution decline in nontreponemal titer used to define response at 1 year after treatment.

Failure of nontreponemal test titers to decline fourfold within 6 months after therapy for primary or secondary

syphilis might be indicative of probable treatment failure. Persons for whom titers remain serofast should be reevaluated for HIV infection. Optimal management of such patients is unclear. At a minimum, these patients should receive additional clinical and serologic follow-up. HIV-infected patients should be evaluated more frequently (i.e., at 3-month intervals instead of 6-month intervals). If additional follow-up cannot be ensured, re-treatment is recommended. Because treatment failure might be the result of unrecognized CNS infection, many specialists recommend CSF examination in such situations.

For retreatment, the majority of STD specialists recommend administering weekly injections of benzathine penicillin G 2.4 million units IM for 3 weeks, unless CSF examination indicates that neurosyphilis is present. In rare instances, serologic titers do not decline despite a negative CSF examination and a repeated course of therapy. Additional therapy or repeated CSF examinations are not warranted in these circumstances.

Latent Syphilis

Treatment

The following regimens are recommended for penicillin nonallergic patients who have normal CSF examinations (if performed).

Recommended Regimens for Adults

Early Latent Syphilis
Benzathine penicillin G 2.4 million units IM in a single dose

Late Latent Syphilis or Latent Syphilis of Unknown Duration
Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Other Management Considerations

All persons who have latent syphilis should be evaluated clinically for evidence of tertiary disease (e.g., aortitis and gumma) and syphilitic ocular disease (e.g., iritis and uveitis). Patients who have syphilis and who demonstrate any of the following criteria should have a prompt CSF examination:

- neurologic or ophthalmic signs or symptoms,
- evidence of active tertiary syphilis (e.g., aortitis and gumma),
- treatment failure, or
- HIV infection with late latent syphilis or syphilis of unknown duration.

If dictated by circumstances and patient preferences, a CSF examination may be performed for patients who do not meet these criteria. Some specialists recommend performing a CSF examination on all patients who have latent syphilis and a nontreponemal serologic test of ≥1:32 or if the patient is HIV-infected with a serum CD4 count ≤350. However, the likelihood of neurosyphilis in this circumstance is unknown. If a CSF examination is performed and the results indicate abnormalities consistent with neurosyphilis, the patient should be treated for neurosyphilis.

If a patient misses a dose of penicillin in a course of weekly therapy for late syphilis, the appropriate course of action is unclear. Pharmacologic considerations suggest that an interval of 10–14 days between doses of benzathine penicillin for late syphilis or latent syphilis of unknown duration might be acceptable before restarting the sequence of injections. Missed doses are not acceptable for pregnant patients receiving therapy for late latent syphilis; pregnant women who miss any dose of therapy must repeat the full course of therapy.

Follow-Up. Quantitative nontreponemal serologic tests should be repeated at 6, 12, and 24 months. Patients with a normal CSF examination should be re-treated for latent syphilis if 1) titers increase fourfold, 2) an initially high titer (≥1:32) fails to decline at least fourfold (i.e., two dilutions) within 12–24 months of therapy, or 3) signs or symptoms attributable to syphilis develop. In rare instances, despite a negative CSF examination and a repeated course of therapy, serologic titers might still not decline. In these circumstances, the need for additional therapy or repeated CSF examinations is unclear.

Neurosyphilis

Treatment

CNS involvement can occur during any stage of syphilis. A patient who has clinical evidence of neurologic involvement with syphilis (e.g., cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms or signs of meningitis) should have a CSF examination.

Syphilitic uveitis or other ocular manifestations frequently are associated with neurosyphilis; patients with these symptoms should be treated according to the recommendations for patients with neurosyphilis. A CSF examination should be performed for all such patients to identify those with abnormalities that require follow-up CSF examinations to assess treatment response.

Patients who have neurosyphilis or syphilitic eye disease (e.g., uveitis, neuroretinitis, and optic neuritis) should be treated with the following regimen.

Recommended Regimen

Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days

If compliance with therapy can be ensured, patients may be treated with the following alternative regimen.

Alternative Regimen

Procaine penicillin 2.4 million units IM once daily
PLUS
Probenecid 500 mg orally four times a day, both for 10–14 days

The durations of the recommended and alternative regimens for neurosyphilis are shorter than that of the regimen used for late syphilis in the absence of neurosyphilis. Therefore, some specialists administer benzathine penicillin, 2.4 million units IM once per week for up to 3 weeks after completion of these neurosyphilis treatment regimens to provide a comparable total duration of therapy.

Other Management Considerations

Other considerations in the management of patients who have neurosyphilis are as follows:

- All patients who have syphilis should be tested for HIV.
- Many specialists recommend treating patients who have evidence of auditory disease caused by syphilis in the same manner as patients who have neurosyphilis, regardless of CSF examination results. Although systemic steroids are used frequently as adjunctive therapy for otologic syphilis, such drugs have not been proven beneficial.

Follow-Up. If CSF pleocytosis was present initially, a CSF examination should be repeated every 6 months until the cell count is normal. Follow-up CSF examinations also can be used to evaluate changes in the VDRL-CSF or CSF protein after therapy; however, changes in these two parameters occur more slowly than cell counts, and persistent abnormalities might be less important. If the cell count has not decreased after 6 months or if the CSF is not normal after 2 years, retreatment should be considered. Recent data on HIV-infected persons with neurosyphilis suggest that CSF abnormalities might persist for extended periods in these persons, and close clinical follow-up is warranted.

Syphilis Among HIV-Infected Persons

Diagnostic Considerations

Unusual serologic responses have been observed among HIV-infected persons who have syphilis. The majority of reports have involved serologic titers that were higher than expected, but false-negative serologic test results and delayed appearance of seroreactivity also have been reported. However, unusual serologic responses are uncommon, and the majority of specialists believe that both treponemal and nontreponemal serologic tests for syphilis can be interpreted in the usual manner for the majority of patients who are coinfected with *T. pallidum* and HIV.

When clinical findings are suggestive of syphilis but serologic tests are nonreactive or their interpretation is unclear, alternative tests (e.g., biopsy of a lesion, darkfield examination, or DFA staining of lesion material) might be useful for diagnosis. Neurosyphilis should be considered in the differential diagnosis of neurologic disease in HIV-infected persons.

Treatment

Compared with HIV-negative patients, HIV-positive patients who have early syphilis might be at increased risk for neurologic complications and might have higher rates of treatment failure with currently recommended regimens. The magnitude of these risks is not defined precisely but is likely minimal. No treatment regimens for syphilis have been demonstrated to be more effective in preventing neurosyphilis in HIV-infected patients than the syphilis regimens recommended for HIV-negative patients. Careful follow-up after therapy is essential.

Primary and Secondary Syphilis Among HIV-Infected Persons

Treatment

Treatment with benzathine penicillin G, 2.4 million units IM in a single dose is recommended. Some specialists recommend additional treatments (e.g., benzathine penicillin G administered at 1-week intervals for 3 weeks, as recommended for late syphilis) in addition to benzathine penicillin G 2.4 million units IM.

Other Management Considerations

Because CSF abnormalities (e.g., mononuclear pleocytosis and elevated protein levels) are common in patients with early syphilis and in persons with HIV infection, the clinical and prognostic significance of such CSF abnormalities in HIV-infected persons with primary or secondary syphilis is unknown. Although the majority of HIV-infected persons respond appropriately to standard benzathine penicillin therapy, some specialists recommend intensified therapy when CNS syphilis is suspected in these persons. Therefore, some specialists recommend CSF examination before treatment of HIV-infected persons with early syphilis, with follow-up CSF examination conducted after treatment in persons with initial abnormalities.

Follow-Up. HIV-infected persons should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy. Although of unproven benefit, some specialists recommend a CSF examination 6 months after therapy.

HIV-infected persons who meet the criteria for treatment failure (i.e., signs or symptoms that persist or recur or persons who have fourfold increase in nontreponemal test titer) should be managed in the same manner as HIV-negative patients (i.e., a CSF examination and re-treatment). CSF examination and re-treatment also

should be strongly considered for persons whose nontreponemal test titers do not decrease fourfold within 6–12 months of therapy. The majority of specialists would re-treat patients with benzathine penicillin G administered as 3 doses of 2.4 million units IM each at weekly intervals, if CSF examinations are normal.

Special Considerations

Penicillin Allergy. Penicillin-allergic patients who have primary or secondary syphilis and HIV infection should be managed according to the recommendations for penicillin-allergic, HIV-negative patients. The use of alternatives to penicillin has not been well studied in HIV-infected patients.

Latent Syphilis Among HIV-Infected Persons

Diagnostic Considerations

HIV-infected patients who have early latent syphilis should be managed and treated according to the recommendations for HIV-negative patients who have primary and secondary syphilis. HIV-infected patients who have either late latent syphilis or syphilis of unknown duration should have a CSF examination before treatment.

Treatment

Patients with late latent syphilis or syphilis of unknown duration and a normal CSF examination can be treated with benzathine penicillin G, at weekly doses of 2.4 million units for 3 weeks. Patients who have CSF consistent with neurosyphilis should be treated and managed as patients who have neurosyphilis.

Follow-Up. Patients should be evaluated clinically and serologically at 6, 12, 18, and 24 months after therapy. If, at any time, clinical symptoms develop or nontreponemal titers rise fourfold, a repeat CSF examination should be performed and treatment administered accordingly. If during 12–24 months the nontreponemal titer does not decline fourfold, the CSF examination should be repeated and treatment administered accordingly.

Special Considerations

Penicillin Allergy. The efficacy of alternative nonpenicillin regimens in HIV-infected persons has not been well studied. Patients with penicillin allergy whose compliance with therapy or follow-up cannot be ensured should be desensitized and treated with penicillin. These therapies should be used only in conjunction with close serologic and clinical follow-up. Limited clinical studies, along with biologic and pharmacologic evidence, suggest that ceftriaxone might be effective. However, optimal dose and duration of ceftriaxone therapy have not been defined.

Reference

Centers for Disease Control and Prevention, Division of Sexually Transmitted Disease Prevention. *2006 STD Treatment Guidelines*. http://www.cdc.gov/std/treatment/2006/rr5511.pdf

Health Advisory:

Pertussis in St. Louis County

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Health Advisory
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FROM: MARGARET T. DONNELLY
DIRECTOR

SUBJECT: Pertussis in St. Louis County

Reported numbers of pertussis cases in Missouri have increased during 2010. Through November 13, a total of 426 confirmed and probable pertussis cases have been reported statewide, representing a 32.7% increase above the 5-year median for this time period.

The largest numbers of reported cases in 2010 have been from St. Louis County, where 126 confirmed and probable cases have been identified through November 13. (The jurisdictions with the next largest numbers of reported cases for this time period are Kansas City, where a total of 30 cases have been reported, and Howell County, with 27 reported cases.)

Of the 126 pertussis cases reported from St. Louis County, 78 (61.9%) were identified in the last 4 weeks. In addition, 59 (46.8%) of these 126 cases have been in persons 10-17 years of age, and local public health officials have identified at least one pertussis case in 20 St. Louis County schools since September 1, 2010.

Pertussis is highly communicable and can cause severe disease or death in very young children. Health care providers should consider pertussis when evaluating any infant, child, adolescent, or adult with an acute cough illness characterized by prolonged cough or cough with paroxysms, whoop, or post-tussive gagging/vomiting. Infants may present with apnea and/or cyanosis. In addition, health care providers should:

- **Consider pertussis in the differential diagnosis of patients presenting with cough illness.**
- **Evaluate persons for eligibility for Tdap vaccination, and vaccinate as indicated.**
- **Educate people who have or may have close contact with infants about the importance of being up-to-date on pertussis immunization. Encourage parents to keep infants away from individuals with a cough illness.**
- **Immediately report known or suspected pertussis cases to the local public health agency (LPHA), or to the Missouri Department of Health and Senior Services (DHSS) at 800/392-0272.**

Clinical Manifestations

The incubation period of pertussis is commonly 7-10 days, with a range of 4-21 days. The catarrhal stage, lasting 1-2 weeks, begins with mild upper respiratory tract symptoms and progresses to severe cough. The condition can further progress to a paroxysmal stage lasting 1-6 weeks, and characterized with inspiratory whoop followed by vomiting. Fever is absent or minimal. In infants younger than six months, apnea is a common manifestation and the whoop may be absent. In the convalescent stage, recovery is gradual. The cough becomes less paroxysmal and disappears in 2-3 weeks. However, paroxysms often recur with subsequent respiratory infections for many months after the onset of pertussis.

Adolescents and adults, and children partially protected by the vaccine, may become infected with *Bordetella pertussis* but have milder disease than infants and young children. Pertussis infection in these persons may be asymptomatic, or present as illness ranging from a mild cough illness to classic pertussis with persistent cough (i.e., lasting more than 7

days). Inspiratory whoop is not common. Pertussis should be considered in older children and adults who have a persistent cough lasting more than 7-14 days, and which cannot be attributed to another specific illness. If untreated, these older children and adults can act as a reservoir for *B. pertussis* and infect younger children.

Diagnostic Testing

The only pertussis diagnostic tests endorsed by the Centers for Disease Control and Prevention (CDC) are culture and polymerase chain reaction (PCR).

Culture is considered the gold standard laboratory test and is the most specific of the laboratory tests for pertussis. Obtaining a positive culture result from a person with pertussis can be affected by several factors, such as how the specimen is handled, the stage of illness at the time of specimen collection, the use of antimicrobial therapy prior to culture, immunity from past infection or from vaccination, and age of the case-patient. Specimens from the posterior nasopharynx, not the throat, should be obtained using Dacron® or calcium alginate (not cotton) swabs. Isolation rates are highest during the first 3 weeks of illness.

PCR should be used in addition to, and not as a replacement for, culture. No PCR product has been approved by the Food and Drug Administration (FDA). The PCR test could be positive beyond the three-week period.

Serologic testing could be useful for adults and adolescents who present late in the course of their illness, when both culture and PCR are likely to be negative. However, there is no FDA-approved diagnostic test. At this time, serologic test results should not be relied upon for case confirmation of pertussis infection.

If a case patient is symptomatic in the absence of another cause and is a close contact of a confirmed pertussis case, DHSS does not recommend testing before treating the case-patient.

Pertussis test kits, including swabs and transport media, can be obtained from LPHAs, or from the Missouri State Public Health Laboratory (573/751-3334).

Treatment

Specific treatment recommendations are available in the American Academy of Pediatrics' *Red Book*. The *Red Book* and CDC recommend erythromycin as well as the new macrolides, clarithromycin or azithromycin dehydrate, as the antimicrobial agents for treatment or prophylaxis against pertussis. A possible alternative for patients who do not tolerate erythromycin is trimethoprim-sulfamethoxazole (TMP-SMZ). Once into the paroxysmal stage, antibiotics will not ameliorate the disease but will limit the spread to others.

If appropriate antimicrobial therapy is contraindicated or the patient refuses treatment, the patient should be isolated until three weeks after the onset of paroxysms. LPHAs can provide epidemiological consultation when required.

Prophylaxis of Household and Other Close Contacts

Chemoprophylaxis is recommended for all household and other close contacts regardless of age, whether or not the contact has pertussis-like symptoms, and irrespective of the contact's immunization status. Close contacts are defined as those persons having direct contact with respiratory, oral, or nasal secretions from a symptomatic case-patient; having direct face-to-face contact, regardless of duration, with a symptomatic case; or having shared a confined space in close proximity for a prolonged period of time with a symptomatic case.

Pertussis in Schools and Child-Care Facilities

Management of pertussis in schools and child-care facilities requires:

1. Identification, evaluation, and treatment of cases.
    - Immediate notification of the LPHA (or DHSS) and, if the case attends or works in a school, the school nurse. Contact information for LPHAs is available at http://www.dhss.mo.gov/LPHA/PublicHealthAgencies.html.

- Collection of a nasopharyngeal specimen for detection of *B. pertussis.*
- Appropriate treatment of cases.

2. Identification of close contacts and high-risk contacts. (Close contacts were defined above. High-risk contacts are persons at risk for developing severe disease and adverse outcomes.)
3. Chemoprophylaxis for all close contacts. In addition, chemoprophylaxis for high-risk contacts who are not close contacts should be considered and evaluated on a case-by-case basis.
4. Initiation of active surveillance for pertussis in the child-care center or school, and continuation of surveillance until six weeks after cough onset of the last confirmed or suspected case. In schools where outbreaks are occurring, implement a **school policy of student exclusion for cough illness** until pertussis is ruled out or an alternative diagnosis is established, or suspected cases have been on appropriate antimicrobial treatment for at least five days. School nurses should require notes from medical providers confirming negative pertussis test results or an alternative diagnosis, or treatment documentation, before ill students can be re-admitted to schools.
5. Assessment of the immunization status of students and staff, and immunization as needed.

Immunization

The best way to reduce the incidence of pertussis is to have a highly vaccinated population, and to that end physicians' offices play a crucial role.

Close contacts under the age of seven years who are unimmunized or underimmunized should have pertussis immunization initiated or continued according to the recommended schedule. Children who received their third dose six months or more before exposure should be given a fourth dose at this time as a protective measure. Children who received their fourth dose three or more years before exposure and who are younger than seven years of age should be given a fifth dose of DTaP at this time.

In the event of an outbreak, it is even more important that a booster Tdap vaccination be given to persons 11-18 years of age if they have not previously received Tdap. Adults 19-64 years of age should receive a single dose of Tdap if it has been more than two years since their last Td vaccine, and they have not previously received Tdap. Shorter intervals can be considered if necessary.

In households with infant(s) less than twelve months of age, all children in the household should be up-to-date with the recommended doses of DTaP and all adults (including the mother) and adolescent household contacts should be appropriately vaccinated with a dose of Tdap, if they have not previously received Tdap.

Any woman who might become pregnant is encouraged to receive a single dose of Tdap if she has not already received a dose. Women who have not received Tdap (including women who are breastfeeding) should receive a dose in the immediate postpartum period, before discharge from the hospital or birthing center, if 2 years or more have elapsed since the last Td. Shorter intervals since the last Td can be used if necessary. If Tdap cannot be administered before discharge, it should be given as soon as feasible. The dose of Tdap replaces the next routine dose of Td.

Finally, it should be remembered that immunized children and adults can still get pertussis.

Reporting

Health care providers are requested to assist in the control of pertussis through immediate reporting of suspect cases by telephone to their LPHA, or to DHSS (800/392-0272).

Questions on pertussis immunization should be directed to DHSS' Bureau of Immunization Assessment and Assurance at 573/751-6124 or 800/219-3224. Other questions should be directed to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113 or 866/628-9891.

References

1. Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine - Preventable Diseases*. Atkinson W, Wolfe S, Hamborsky J, McIntyre L, eds. "Pertussis." 11th Ed. Washington DC: Public Health Foundation, 2009, 199 – 216.
   (Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm)
2. Centers for Disease Control and Prevention. Prevention of Pertussis, Diphtheria and Tetanus among Pregnant and Postpartum Women and their Infants. *Morbidity and Mortality Weekly Report*, 2008;57(No.RR-4).
   (Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5704a1.htm)
3. Academy of Pediatrics. "Pertussis". In: Pickering L, ed. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 27th Ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: 504 – 519.

DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine

Tdap = tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine

Td = tetanus and diphtheria toxoids vaccine

Health Advisory:

Guidance for Clinicians on the Use of Rapid Influenza Diagnostic Tests

December 22, 2010

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies, and/or the public.

Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

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Health Advisory
December 22, 2010

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Guidance for Clinicians on the Use of Rapid Influenza Diagnostic Tests (RIDTs)**

The Centers for Disease Control and Prevention (CDC) has recently made available a 13-page document entitled *Guidance for Clinicians on the Use of Rapid Influenza Diagnostic Tests for the 2010-2011 Influenza Season*. It provides a detailed summary of rapid influenza diagnostic tests (RIDTs), including recommendations for their use. This document is available at http://www.cdc.gov/flu/pdf/professionals/diagnosis/clinician_guidance_ridt.pdf. The following are some of the key points.

RIDTs are immunoassays that can identify the presence of influenza A and B viral nucleoprotein antigens in respiratory specimens, and display the result in a qualitative way (positive vs. negative). In the United States, a number of RIDTs are commercially available. Some of these tests distinguish between influenza A or B virus infection, while others do not. RIDTs that provide results on type of influenza virus (e.g. influenza A or B virus), do not provide information on influenza A virus subtype (e.g. A/H1N1 versus A/H3N2) or specific strain information.

RIDTs can yield results in a clinically relevant time frame, i.e., approximately 15 minutes or less. However, RIDTs have limited sensitivity to detect influenza virus infection and negative test results should be interpreted with caution given the potential for false-negative results. False-negative (and true-positive) results are more likely to occur when disease prevalence is high in the community.

Although the specificities of RIDTs are generally high, false-positive results can be seen. False-positive (and true-negative) results are more likely to occur when disease prevalence in the community is low.

To minimize false results:

- Collect specimens as early in the illness as possible (ideally < 4 days from illness onset).
- Follow manufacturer's instructions, including acceptable specimens, and handling.
- Follow-up negative results with confirmatory tests (RT-PCR or viral culture) if a laboratory-confirmed influenza diagnosis is desired.

RIDTs may be used to help with diagnostic and treatment decisions for patients in clinical settings, such as whether to prescribe antiviral medications. However, due to the limited sensitivities and predictive values of RIDTs, negative results of RIDTs do not exclude influenza virus infection in patients with signs and symptoms suggestive of influenza. Therefore, appropriate antiviral treatment should not be withheld from patients with suspected influenza even if they test negative. (Influenza antiviral treatment recommendations are available at http://www.cdc.gov/flu/professionals/antivirals/.) Note also that testing is not needed for all patients with signs and symptoms of influenza to make antiviral treatment decisions. Once influenza activity has been documented in the community or geographic area, a clinical diagnosis of influenza can be made for outpatients with signs and symptoms consistent with suspected influenza, especially during periods of peak influenza activity in the community.

Questions on RIDTs should be directed to the Missouri State Public Health Laboratory (MSPHL) at 573/751-3334. Medical epidemiology support is available for medical consultations regarding influenza clusters, outbreaks, and clinical testing. Please contact the DHSS Epidemic Intelligence Service (EIS) officer, Philip Lo, MD, at Philip.lo@dhss.mo.gov, or 573/526-1369 (days) or 800/392-0272 (nights, weekends, holidays) for such consultation.